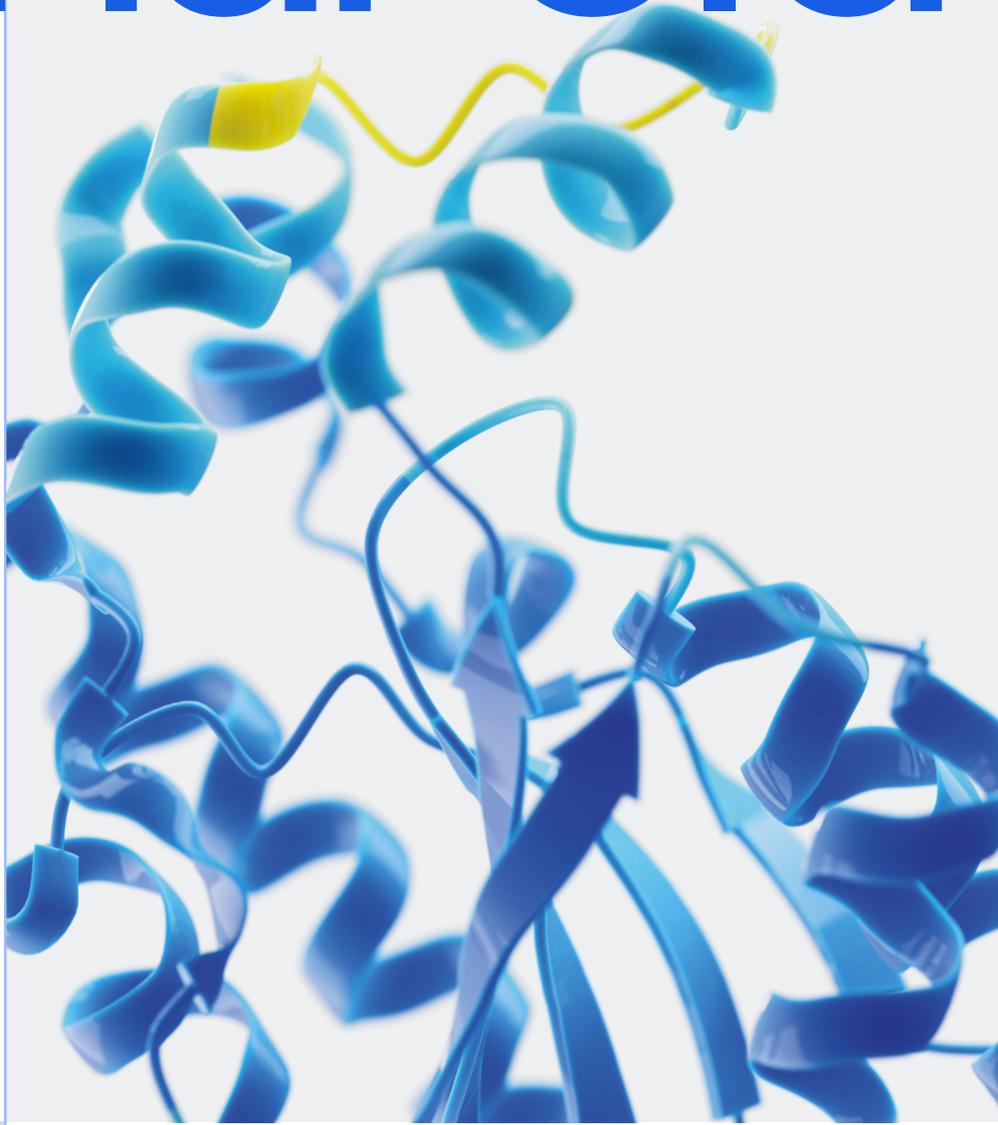


AlphaFold



Revealing a Missing
Link in **Viral Evolution**

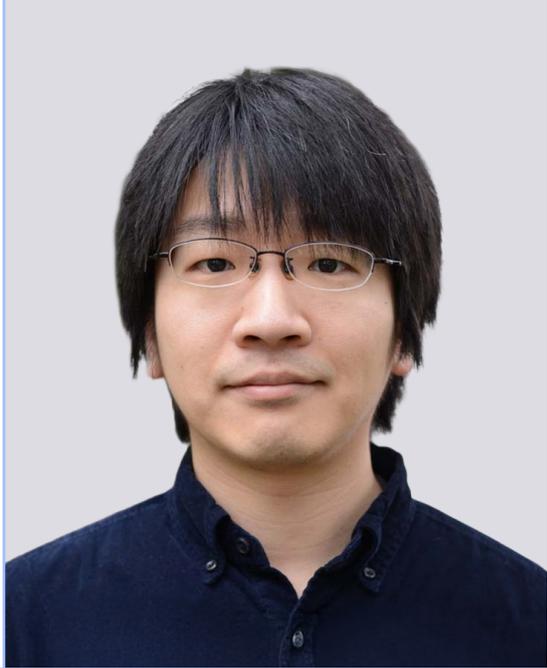
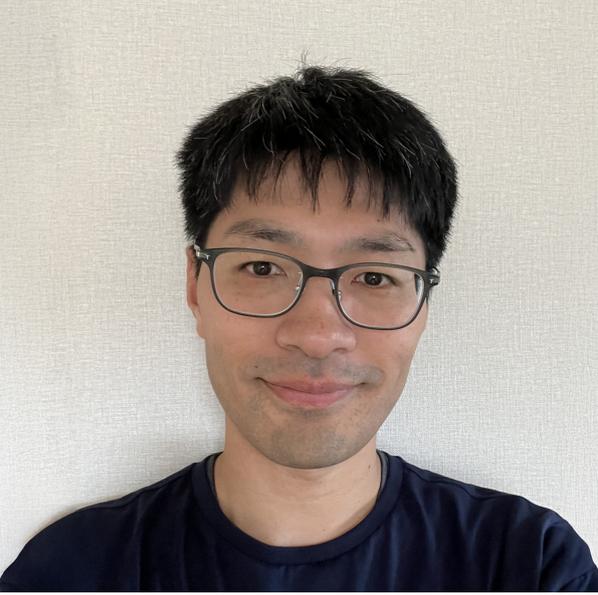
How AlphaFold helped scientists uncover a new lineage of RNA viruses in Japan's hot springs

For years, RNA viruses were thought to exist mainly in plants, animals, and fungi. But what about the microscopic worlds thriving in Japan's hot springs? These extreme environments, rich in microbial life, remained largely unexplored because the RNA viruses living there are incredibly hard to study. Their genetic material often degrades under high acidity and heat, and their proteins tend to be unstable or completely novel, making them nearly impossible to analyze using standard lab techniques.



Dr. Syun-ichi Urayama's team at the University of Tsukuba embarked on the challenge of uncovering these "hidden" viruses through a series of environmental sampling and metatranscriptomic sequencing – a digital process that reads all the RNA in a sample to identify which viruses or microbes are active. From this data, researchers detected genes encoding unusual enzymes known as RNA-dependent RNA polymerases (RdRPs), key molecules used by RNA viruses to replicate their genetic material.

The team turned to AlphaFold to better understand how these mysterious viral proteins might work. By using AI to predict the 3D structures of these newly identified proteins, they discovered that some of them shared a hidden structural similarity with known enzyme families of RdRP. This helped them trace possible evolutionary links between the new viruses and existing ones, confirming a shared ancestry and revealing a previously hidden, widespread family of life across diverse ecosystems that could not have been recognized from genetic data alone.



“When we first looked at the sequence, it didn’t resemble any known RNA polymerase,” recalled Dr. Akihito Fukudome of Howard Hughes Medical Institute/Indiana University, who collaborated with Dr. Urayama’s team. “But once we ran it through AlphaFold, the shape became clear – it really was a polymerase, but with unique features we hadn’t seen before. That was a very exciting moment.”

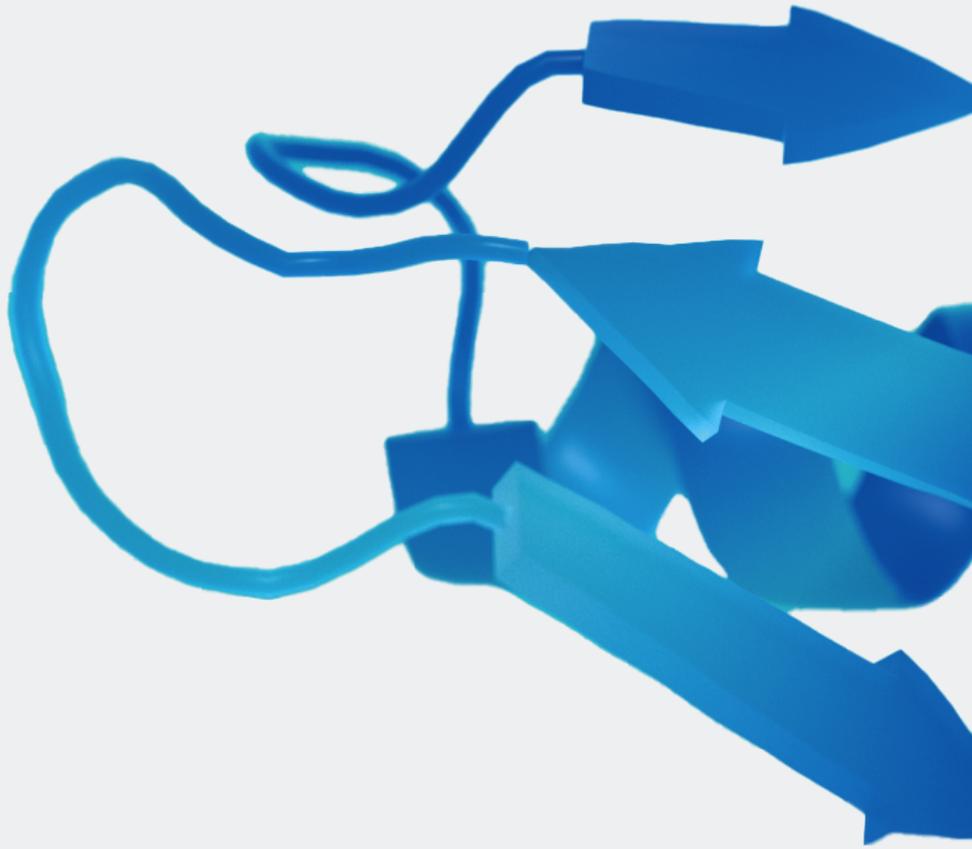
“Without AlphaFold, we would have had to determine the structure of each protein experimentally. That process can take months, or even years. With AlphaFold, we could move straight to analysis,” said Dr. Urayama.

Striking a balance

The combination of AI predictions and experimental validation was vital in allowing Dr. Urayama, Dr. Fukudome, and their teams to focus on the most promising proteins, which in turn cut months of lab time and resource cost. AlphaFold’s accessibility also allowed the Japanese researchers to bridge computational and field-based microbiology easily.

While both Dr. Urayama and Dr. Fukudome agree that AlphaFold plays a transformative role in research, they emphasized that AI should be seen as a starting point, not an end point. In their experience, cross-checking the models with other tools to ensure accuracy is essential.

“Interpretation still needs a structural biologist’s eye,” notes Dr. Fukudome.



Looking to the future

At present, Prof. Urayama's team is studying a newly detected group of self-replicating RNA molecules from Japan's hot springs. These "circular RNAs" are self-replicating molecules that encode previously unknown proteins, and could possibly represent an unexplored branch in the story of molecular evolution. With AlphaFold in hand, researchers are able to learn more about how these molecules function and evolve.

Urayama notes that AI is becoming increasingly embedded across every step of research, from structural predictions to data analysis, helping shorten processes that once took months. "Not just with AlphaFold, but also with conventional research methods, AI can be applied at that step," he explained. "I don't think there's any option not to use AI. The real challenge now is learning how best to use it alongside conventional research methods."

This is reflective of the growing balance between microbiology and AI breakthroughs in Japan's research landscape, and a true testament to how innovation can accelerate discovery in any environment.